Coffee, Tea, and Cocoa and Risk of Stroke

Susanna C. Larsson, PhD

Coffee, tea, and cocoa are important dietary sources of polyphenols and have received much attention during the past years because of their potential beneficial effects on cardiovascular health. The polyphenols in these beverages and cocoa may reduce the risk of stroke through multiple mechanisms, including antihypertensive, hypcholesterolemic, antioxidant, and anti-inflammatory effects as well as through improvements of vascular endothelial function and insulin sensitivity. This review summarizes the available evidence from experimental studies, prospective studies, and meta-analyses of the potential role of coffee, tea, and cocoa in the prevention of stroke.

Methods

References for this review were identified through a literature search of the PubMed database through October 2013 by using the following search terms: coffee, tea, cocoa, prospective study, cohort study, randomized trial, meta-analysis, review, stroke, cerebral infarction, and cerebrovascular disease. Moreover, the reference lists of pertinent publications were searched manually for further relevant articles. Priority was given to systematic reviews and meta-analyses published during the past 5 years. When >1 meta-analysis on the same topic was available, the most recent publication was included in the present review.

Coffee

Coffee is a complex beverage with hundreds of bioactive components with potential adverse or beneficial effects on the cardiovascular system. The most abundant bioactive compounds in coffee are caffeine, diterpenes (present in the oil), and polyphenols. The cardiovascular effects of coffee drinking depend in part on coffee preparation method and individual characteristics (eg, hypertension and hyperlipidemia).1–3 There are 2 main methods of coffee preparation: filtered and unfiltered. Filtered coffee, also known as drip-brewed coffee, is the most common mode of preparation in the United States and involves brewing the coffee through a paper filter. Unfiltered coffee, often known as boiled coffee, do not use a filter and includes Scandinavian boiled, French press, Turkish/Greek, and espresso coffees. Espresso contains negligible amounts.6 In a meta-analysis of 12 RCTs, including 1017 subjects, consumption of unfiltered coffee significantly increased total cholesterol, low-density lipoprotein (LDL) cholesterol, and triglyceride concentrations, whereas filtered coffee consumption produced a small change in total cholesterol concentrations only (Table 1). The meta-analysis further showed that those who had hyperlipidemia seemed to be more sensitive to the cholesterol-raising effect of coffee.4

Coffee is rich in various polyphenols, most notably chlorogenic acid (CGA), which possesses antioxidant activities in vitro.7 Studies in animals have demonstrated that coffee and caffeic acid, a primary CGA metabolite, can decrease lipid peroxidation, thus indicating also an in vivo antioxidant activity.7 However, there is controversy on whether chlorogenic acid and other polyphenols in coffee could suppress the oxidative modification of LDL particles in humans. Among 3 available studies on this topic, 2 studies reported a protective effect of 1 cup of boiled6 or filtered coffee7 on LDL oxidation, whereas 1 study found neither short-term nor long-term effects of filtered coffee consumption on lipid peroxidation.10 As opposed to caffeine, CGA have been demonstrated to have antihypertensive effects,11,12 possibly via nitric oxide–mediated vasodilation.12 Results from an RCT of 23 healthy adults showed that CGA ingestion significantly reduced systolic blood pressure by 2.41 mm Hg and diastolic blood pressure by 1.53 mm Hg.12

Epidemiological Studies on Coffee and Stroke

In the past, coffee was generally viewed as a risk factor for cardiovascular disease. However, recent evidence suggests that moderate coffee consumption may reduce stroke risk. Results from a meta-analysis of 11 prospective studies (published through January 2011) involving 479689 participants and 10003 stroke cases showed a nonlinear relationship between coffee consumption and stroke risk.
(Figure 1). Compared with no coffee consumption, the overall relative risks (RRs; 95% CI) of total stroke were 0.87 (0.81–0.93) for 2, 0.84 (0.77–0.91) for 3–4, 0.88 (0.79–0.97) for 6, and 0.94 (0.80–1.10) for 8 cups/d of coffee. Risk estimates were similar for ischemic and hemorrhagic stroke and for men and women at lower levels of coffee consumption (≤2 cups/d). Three prospective studies on coffee consumption and stroke were published since the meta-analysis. Two of them confirmed an inverse association between moderate coffee consumption and stroke risk (RR, 0.87; 95% CI [0.81–0.93]), for ≥2 cups/d versus none). No association between caffeinated or decaffeinated coffee consumption and stroke risk was observed in a prospective study of 42,659 German adults, but the number of cases was small (n=310). Coffee consumption is usually associated with a less health conscious diet and lifestyle. Although most studies controlled for other dietary and lifestyle factors, residual confounding may in part explain the inconsistent results. Furthermore, breast the relative composition of bioactive compounds in coffee varies by coffee preparation method, this could contribute to the heterogeneity among studies in different populations.

### Green and Black Tea

Tea is the most frequently consumed beverage in the world after water. Tea is produced from the leaves of the plant *Camellia sinensis* and can be classified by degree of fermentation: black tea (fermented), predominantly consumed in Western countries; oolong tea (partially fermented), primarily consumed in Southern China and Taiwan; and green tea (unfermented), mainly consumed in Asia. All types of tea are rich in various flavonoids. Catechins are the main flavonoids in green tea, whereas black tea mainly contains condensed flavonoids, such as theaflavins and thearubigins. These tea and tea-derived flavonoids have been demonstrated to have a hypocholesterolemic effect and to reduce the development of atherosclerosis in animal models. Tea flavonoids can enhance nitric oxide status and improve endothelial function, which could at least partly be responsible for the benefits of tea on cardiovascular health.

Studies in humans also indicate potential beneficial effects of consumption of green and black tea on cardiometabolic risk factors, including endothelial function (measured by flow-mediated dilatation), blood pressure, and cholesterol and blood glucose concentrations. In a meta-analysis of 9 RCTs (2 on green tea, 6 on black tea, and 1 on both types of tea), involving 213 participants, the overall absolute increase in FMD of tea consumption (median daily dose of 500 mL tea, equivalent to 2–3 cups) versus placebo was 2.6% of the arterial diameter. This is a relative improvement of ≈40% compared with the average FMD of 6.3% measured under placebo or baseline conditions. Results from a meta-analysis of 14 short-term (≤3 months) RCTs showed that green tea consumption lowered total and LDL cholesterol.

### Table 1. Summary of Recent Meta-Analyses of RCTs of the Effects of Coffee or Caffeine Intake on Cardiometabolic Biomarkers

<table>
<thead>
<tr>
<th>References</th>
<th>Interventions</th>
<th>Duration</th>
<th>No. of Trials</th>
<th>Outcomes</th>
<th>Effects</th>
<th>Mean Change</th>
<th>Heterogeneity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mesas et al, 2011</td>
<td>Coffee or caffeine (200–300 mg)</td>
<td>&lt;60–180 min</td>
<td>5</td>
<td>SBP (mmHg)</td>
<td>↓</td>
<td>8.14 (5.68, 10.61)</td>
<td>0.99</td>
</tr>
<tr>
<td>Steffen et al, 2012</td>
<td>Filtered, boiled, instant, or decaffeinated coffee</td>
<td>4–16 wk</td>
<td>10</td>
<td>SBP (mmHg)</td>
<td>↔</td>
<td>0.55 (–2.46, 1.36)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Cai et al, 2012</td>
<td>Filtered coffee</td>
<td>14–79 d</td>
<td>10</td>
<td>Total cholesterol (mmol/L)*</td>
<td>↓</td>
<td>0.09 (0.02, 0.17)</td>
<td>0.52</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>LDL cholesterol (mmol/L)*</td>
<td>↔</td>
<td>0.06 (–0.03, 0.15)</td>
<td>0.35</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Triglycerides (mmol/L)*</td>
<td>↔</td>
<td>0.04 (–0.05, 0.13)</td>
<td>0.43</td>
</tr>
<tr>
<td>Cai et al, 2012</td>
<td>Boiled/unfiltered coffee</td>
<td>14–79 d</td>
<td>12</td>
<td>Total cholesterol (mmol/L)*</td>
<td>↓</td>
<td>0.33 (0.18, 0.49)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>LDL cholesterol (mmol/L)*</td>
<td>↓</td>
<td>0.31 (0.08, 0.53)</td>
<td>0.002</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Triglycerides (mg/dL)*</td>
<td>↑</td>
<td>0.21 (0.05, 0.37)</td>
<td>0.001</td>
</tr>
</tbody>
</table>

CI indicates confidence interval; DBP, diastolic blood pressure; LDL, low-density lipoprotein; RCTs, randomized controlled trials; and SBP, systolic blood pressure.

*Values were converted from mg/dL to mmol/L by dividing the levels of cholesterol (total, LDL, and HDL) by 38.67; triglyceride levels by 88.57; and glucose levels by 18.02.

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**Figure 1.** Relative risks of stroke by coffee consumption in prospective studies. The relative risks were extracted from the meta-analysis by Larsson and Orsini. 

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### Table 2. Summary of Recent Meta-Analyses of RCTs of the Effects of Green and Black Tea Consumption on Cardiometabolic Biomarkers

<table>
<thead>
<tr>
<th>References</th>
<th>Interventions</th>
<th>Duration</th>
<th>No. of Trials</th>
<th>Outcomes</th>
<th>Effects</th>
<th>Mean Change (95% CI)</th>
<th>Heterogeneity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ras et al, 2011</td>
<td>Green or black tea as a beverage</td>
<td>≤120 min–4 wk</td>
<td>9</td>
<td>FMD (%)</td>
<td>†</td>
<td>2.6 (1.8, 3.3)</td>
<td>&lt;0.001 75.8</td>
</tr>
<tr>
<td>Zheng et al, 2011</td>
<td>Green tea as a beverage or green tea extract</td>
<td>3 wk–3 mo</td>
<td>14</td>
<td>Total cholesterol (mmol/L)*</td>
<td>↓</td>
<td>−0.19 (−0.21, −0.16)</td>
<td>0.35 9</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>LDL cholesterol (mmol/L)*</td>
<td>↓</td>
<td>−0.06 (−0.08, −0.03)</td>
<td>0.20 25</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>HDL cholesterol (mmol/L)*</td>
<td>↔</td>
<td>0.006 (−0.02, 0.03)</td>
<td>0.27 18</td>
</tr>
<tr>
<td>Hartley et al, 2013</td>
<td>Green tea as a beverage or green tea extract</td>
<td>3–6 mo</td>
<td>2</td>
<td>SBP (mmHg)</td>
<td>↓</td>
<td>−3.18 (−5.25, −1.11)</td>
<td>0.72 0</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>DBP (mmHg)</td>
<td>↓</td>
<td>−3.42 (−4.54, −2.30)</td>
<td>0.39 0</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Total cholesterol (mmol/L)</td>
<td>NA</td>
<td>NA*</td>
<td>84</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>LDL cholesterol (mmol/L)</td>
<td>↔</td>
<td>−0.43 (−0.56, −0.31)</td>
<td>0.22 33</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>HDL cholesterol (mmol/L)</td>
<td>↔</td>
<td>−0.01 (−0.06, 0.04)</td>
<td>0.20 36</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Triglycerides (mmol/L)</td>
<td>NA</td>
<td>NA*</td>
<td>64</td>
</tr>
<tr>
<td>Liu et al, 2013</td>
<td>Black tea extracts, in tablet form or as a drink</td>
<td>3–6 mo</td>
<td>2</td>
<td>SBP (mmHg)</td>
<td>↓</td>
<td>−1.85 (−3.21, −0.48)</td>
<td>0.49 0</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>DBP (mmHg)</td>
<td>↔</td>
<td>−1.27 (−3.06, 0.53)</td>
<td>0.53 0</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Total cholesterol (mmol/L)</td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td>HDL cholesterol (mmol/L)</td>
<td>↔</td>
<td>−0.05 (−0.37, 0.26)</td>
<td>0.31 16</td>
</tr>
</tbody>
</table>

CI indicates confidence interval; DBP, diastolic blood pressure; FMD, flow-mediated dilation; Hb A<sub>1c</sub>, glycohemoglobin; HDL, high-density lipoprotein; HOMA-IR, homeostatic model assessment index for insulin resistance; LDL, low-density lipoprotein; NA, not available; RCTs, randomized controlled trials; and SBP, systolic blood pressure.

*Meta-analysis was not performed because of significant heterogeneity between the trials.

†Values were converted from mg/dL to mmol/L by dividing by 38.67 for total cholesterol, LDL cholesterol, and HDL cholesterol; by 88.57 for triglycerides; and by 18.02 for glucose.
concentrations but had no effect on high-density lipoprotein cholesterol.20 In another meta-analysis of RCTs of ≥3 months duration, both green and black tea consumption reduced LDL cholesterol concentrations as well as BP.21 With regard to glucose and insulin, 2 meta-analyses of several RCTs found that green tea consumption decreased fasting blood glucose concentrations, whereas results for insulin and hemoglobin A1c concentrations were inconsistent.22,23

Epidemiological Studies on Tea and Stroke

In a meta-analysis of 14 prospective studies of green or black tea consumption, the overall RR of total stroke for a 3-cup/d increment in tea consumption was 0.87 (95% CI, 0.81–0.94), with heterogeneity among studies (P=0.006).24 There was no evidence of publication bias (Egger test: P=0.85).26 The association was similar in men and women and among most subgroups, but was slightly stronger for green tea (RR=0.83; 95% CI [0.72–0.96]; P_heterogeneity<0.01; n=5 studies) than for black tea (RR=0.91; 95% CI [0.83–0.98]; P_heterogeneity=0.17; n=13 studies).24 The heterogeneity may be because of differences in types of tea, tea preparation methods (amounts of tea leaves, cup size, brewing time, water temperatures, addition of milk or sugar, etc), stroke measures, and analysis strategies.24

Two recent large prospective studies of green14 or black tea25 consumption confirmed a reduction in stroke risk associated with high tea consumption. Results from a cohort of 82,369 Japanese men and women showed a significant 20% reduced risk of total stroke among those who consumed ≥4 cups/d of green tea.14 In a cohort of 74,961 Swedish men and women, consumption of ≥4 cups/d of black tea, compared with no consumption, was associated with a significant 21% lower risk of total stroke.25 In both studies, the association was similar for ischemic stroke and intracerebral hemorrhage.

Cacao Products

Cacao products, such as chocolate, are rich sources of flavonoids, mainly flavan-3-ols (also referred to as flavanols), which are potent...
antioxidant and anti-inflammatory compounds. Both the flavan-3-ol content and the total antioxidant capacity in plasma increase after cocoa consumption. Whether these effects are reduced when cocoa is ingested with milk or when cocoa is consumed as milk chocolate is controversial. Flavanols found in cocoa have also been shown to increase the formation of endothelial nitric oxide, which promotes vasodilation and thus blood pressure reduction.

The potential benefits of cocoa products on cardiovascular health have been examined in several short-term RCTs, and results from those trials have been summarized in meta-analyses. The overall results from 2 meta-analyses indicate that cocoa or chocolate intake may modestly reduce systolic blood pressure and diastolic blood pressure, but findings from individual trials were inconsistent (Table 3). A recent meta-analysis of 42 acute or short-term chronic RCTs found that cocoa or chocolate interventions significantly reduced fasting insulin concentrations, insulin resistance, and mean arterial pressure as well as improved endothelial function measured by FMD (Table 3). Cocoa or chocolate consumption had only marginally significant or no effects on blood concentrations of cholesterol (total, LDL, and high-density lipoprotein), triglycerides, glucose, hemoglobin A1c, and C-reactive protein. In a recent 1-year trial comprising 95 postmenopausal women with type 2 diabetes mellitus, a combination of flavan-3-ols and isoflavones reduced LDL cholesterol (−0.1 mmol/L; P=0.04) and insulin (−0.8 mU/L; P=0.02) concentrations and the homeostatic model assessment index for insulin resistance (−0.3; P=0.004).

Several controlled intervention studies have found that flavanols present in cocoa may improve platelet aggregation. Based on data from 5 trials, Ostertag et al estimated that intake of 100 mg of flavanols induces a 3% to 11% reduction in platelet aggregation.

**Epidemiological Studies on Chocolate and Stroke**

The few prospective studies of chocolate consumption in relation to stroke risk have reported either a statistically significant or a non-significant inverse association (Figure 2). Results from a meta-analysis of those 5 studies (4 from Europe and 1 from the United States) showed a significant 19% lower risk of stroke when comparing the highest with the lowest category of chocolate consumption (Figure 2) and a significant 14% reduction in stroke risk for a 50-g/week increment in chocolate consumption, without heterogeneity among studies. There was indication of potential publication bias in the meta-analysis for the highest versus lowest category of chocolate consumption (Egger test: P=0.03) but not in the dose–response meta-analysis (Egger test: P=0.26).

**Summary**

Current evidence from experimental studies in animals and humans along with findings from prospective studies indicates beneficial effects of green and black tea as well as chocolate on cardiovascular health, and that tea and chocolate consumption may reduce the risk of stroke. The strongest evidence exists for beneficial effects of tea and cocoa on endothelial function, total and LDL cholesterol (tea only), and insulin sensitivity (cocoa only). The majority of prospective studies have reported a weak inverse association between moderate consumption of coffee and risk of stroke. However, there are yet no clear biological mechanisms whereby coffee might provide cardiovascular health benefits. Awaiting the results from further long-term RCTs and prospective studies, moderate consumption of filtered coffee, tea, and dark chocolate seems prudent.

**Disclosures**

None.

**References**


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**Key Words:** cacao ☰ coffee ☰ diet ☰ flavonoids ☰ polyphenols ☰ risk factors ☰ stroke ☰ tea
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Stroke. 2014;45:309-314; originally published online December 10, 2013;
doi: 10.1161/STROKEAHA.113.003131
Stroke is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
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Print ISSN: 0039-2499. Online ISSN: 1524-4628

The online version of this article, along with updated information and services, is located on the
World Wide Web at:
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