Effect of Cocoa and Tea Intake on Blood Pressure

A Meta-analysis

Dirk Taubert, MD, PhD; Renate Roesen, PhD; Edgar Schömig, MD

Background: Epidemiological evidence suggests blood pressure–lowering effects of cocoa and tea. We undertook a meta-analysis of randomized controlled trials to determine changes in systolic and diastolic blood pressure due to the intake of cocoa products or black and green tea.

Methods: MEDLINE, EMBASE, SCOPUS, Science Citation Index, and the Cochrane Controlled Trials Register were searched from 1966 until October 2006 for studies in parallel group or crossover design involving 10 or more adults in whom blood pressure was assessed before and after receiving cocoa products or black or green tea for at least 7 days.

Results: Five randomized controlled studies of cocoa administration involving a total of 173 subjects with a median duration of 2 weeks were included. After the cocoa diets, the pooled mean systolic and diastolic blood pressure were −4.7 mm Hg (95% confidence interval [CI], −7.6 to −1.8 mm Hg; P = .002) and −2.8 mm Hg (95% CI, −4.8 to −0.8 mm Hg; P = .006) lower, respectively, compared with the cocoa-free controls. Five studies of tea consumption involving a total of 343 subjects with a median duration of 4 weeks were selected. The tea intake had no significant effects on blood pressure. The estimated pooled changes were 0.4 mm Hg (95% CI, −1.3 to 2.2 mm Hg; P = .63) in systolic and −0.6 mm Hg (95% CI, −1.5 to 0.4 mm Hg; P = .38) in diastolic blood pressure compared with controls.

Conclusion: Current randomized dietary studies indicate that consumption of foods rich in cocoa may reduce blood pressure, while tea intake appears to have no effect.

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A N INCREASED CONSUMPTION of fruits and vegetables is recommended as a first-line therapeutic approach in current hypertension control guidelines. At least part of the reduction of blood pressure and lowering cardiovascular risk has been attributed to the polyphenols (flavonoids) in fruits and vegetables. Tea and cocoa products account for the major proportion of total polyphenol intake in Western countries. However, cocoa or tea are currently not implemented in cardioprotective or anti-hypertensive dietary advice, although both have been associated with lower incidences of cardiovascular events. A recent cross-sectional study suggests considerable hypotensive and cardioprotective effects of cocoa. Observational studies of the association between consumption of black or green tea and blood pressure yielded mixed results; some have reported a reduction of blood pressure, while others found no effects. These discrepancies may be due to potential biases and confounding factors that are in particular inherent to epidemiological studies of diet and disease. Several randomized controlled trials have also been conducted to answer the question of a causal relationship of cocoa and tea consumption on blood pressure, principally providing higher strength of evidence for an association with a dietary effect. We therefore undertook a prospective meta-analysis of randomized controlled trials to quantitatively assess the effect of cocoa or tea intake on blood pressure.

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METHODS

LITERATURE SEARCH

To identify randomized controlled studies that report the effects of cocoa or tea intake on blood pressure, we searched the electronic databases MEDLINE, EMBASE, SCOPUS, and Science Citation Index from 1966 to October 2006 as well as the Cochrane Controlled Trials Register for the medical subject headings (MeSH) and text words “cocoa,” “chocolate,” “tea,” etc.
“blood pressure,” “hypertension,” “endothelium,” and “cardiovascular.” We also compiled citations from the reference lists of original and review articles. Of the citations identified by the search terms (cocoa) OR (chocolate)/respectively (tea) AND (randomized controlled trial[Publication Type]) OR (randomized[Title/Abstract] AND controlled[Title/Abstract] AND trial[Title/Abstract]), the full articles were retrieved.

STUDY SELECTION

We considered studies in any language that were published as full articles. For inclusion, studies had to fulfill the following criteria: have a randomized controlled parallel group or crossover design; have examined at least 10 normotensive or hypertensive adults (age ≥18 years); report means (or differences between means) and standard deviations or 95% confidence intervals (CIs) of systolic blood pressure (SBP) and diastolic blood pressure (DBP) at baseline and after the intervention; and provide type, duration, and amount of the cocoa or tea consumption. Studies were excluded if only abstracts were published; information on cocoa or tea and control interventions was incomplete; allocation of participants to the treatments was not randomized; only supplements of tea or cocoa ingredients were used; or vitamin supplements or polyphenol-rich foods were concomitantly ingested or cocoa and tea intake was mixed with other dietary treatments. Data of multiple published reports from the same study population were included only once. Furthermore, studies with a duration of less than 7 days were excluded from the analysis. This cutoff value was set because shorter assessments (often only administrations of a single dose of cocoa or tea) were considered of questionable clinical relevance, and none of these very short term studies we retrieved by our search strategy (Figure 1) reported changes in blood pressure after ingestion of cocoa or black and green tea.

DATA EXTRACTION AND QUALITY ASSESSMENT

Data were extracted independently by 2 investigators (D.T. and R.R.) with an interrater agreement value of κ = 0.94, and disagreements were resolved by consensus. Methodological quality of the selected studies was assessed independently by 2 reviewers (D.T. and R.R.) (κ = 0.89), and discrepancies were resolved by consensus. Randomized controlled trials were evaluated using the validated Jadad 11-item instrument with a maximum possible score of 13 points.23 Study quality was considered to be good when the score was greater than 9 points and poor when the score was 9 points or lower.

Extracted data include the first author’s name; year of publication; country of investigation; number, age, sex, and health status of participants; losses to follow-up; concomitant medications; trial design and duration; Jadad score; funding sources; intervention assessment; and assessment of change in mean ± SD SBP and DBP.

DATA SYNTHESIS AND ANALYSIS

Changes in SBP and DBP in cocoa or tea and control groups are reported as differences between arithmetic means before and after intervention. If not reported, standard deviations of these differences were estimated by the following equation:

\[ \text{SD}_{\text{difference}} = \sqrt{ \left( \frac{\text{SD}_{\text{intervention}}^2 + \text{SD}_{\text{control}}^2}{2} \times \text{R} \times \text{SD}_{\text{intervention}} \times \text{SD}_{\text{control}} \right) } \]

For the 2 studies in which subjects’ individual pretreatment and posttreatment blood pressure values were available,20,23 we calculated values of the correlation coefficient R of greater than 0.85 for SBP and greater than 0.90 for DBP. To be conservative, we used an imputed value of R of 0.68 according to the suggestions of the Cochrane Handbook for Systematic Reviews of Interventions. Crossover trials were incorporated in the meta-analysis as paired analyses if individual data were available. Otherwise, measurements from cocoa or tea and control intervention periods were considered in the same way as parallel group trials of cocoa or tea vs control by imputing the change estimates of the standard deviations.

Interstudy heterogeneity was assessed by the Cochrane Q test; \( P < .10 \) was considered statistically significant.
The magnitude of heterogeneity was evaluated by the I² statistic that describes the proportion of total variation in study estimates that is due to heterogeneity.33

To account for interstudy heterogeneity, the pooled estimates of the mean differences in SBP and DBP between control and intervention and the corresponding 95% CIs were calculated by the random effects model according to DerSimonian and Laird.34

Potential publication bias in the meta-analyses was assessed by the funnel plots of each trial's effect size against the inverse standard error. Funnel plot asymmetry was evaluated by the Egger regression test requiring a minimum of 5 trials to reliably detect a bias (P<.10).35 Adjusted estimates of the pooled changes in blood pressure and the overall 95% CIs were calculated by the trim-and-fill method according to Duval and Tweedie.36

To test whether any one study was exerting excessive influence on the results, we conducted a sensitivity analysis by systematically excluding each study and then reanalyzing the remaining data. Additional sensitivity analyses were done to test the influence of alternative values (0 and 1) of the imputed correlation coefficient R on the pooled estimates.

The statistical analyses were performed with Cochrane Review Manager 4.2 (Cochrane Library Software, Oxford, England) and MIX version 1.4 software (Department of Medical Informatics, Kitasato University, Kanagawa, Japan).

We identified 10 studies that met the inclusion criteria, with 5 addressing the relation between cocoa (Table 1) and 5 the relation between tea (Table 2) intake and blood pressure. Most studies were excluded because of short duration (<7 days) or missing information of randomization, withdrawals, or outcome (Figure 1). Two studies were excluded because supplements of cocoa or tea extracts were applied.37,38 One study39 assessed black tea and green tea in the same subjects in subsequent interventions. Because of the lack of independency between these studies and since black tea and green tea did not differ in their effects on blood pressure, we entered only the data of the black tea intervention. The cocoa studies had a combined total of 173 individuals allocated to cocoa (n=87) and control (n=86) arms, and the tea studies had a combined total

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### RESULTS

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### Table 1. Characteristics of Randomized Controlled Trials Examining Blood Pressure Changes Due to Cocoa Intake

<table>
<thead>
<tr>
<th>Source</th>
<th>Study Design, Duration (Subjects’ Inclusion Criteria), Medication</th>
<th>No. of Participants Enrolled (Men/Women), Mean Age (Range), y</th>
<th>Study Quality: Jadad Score, Funding Sources</th>
<th>Intervention</th>
<th>SBP, Mean (SD), mm Hg, Before/After Cocoa Intervention vs Control</th>
<th>DBP, Mean (SD), mm Hg, Before/After Cocoa Intervention vs Control</th>
</tr>
</thead>
<tbody>
<tr>
<td>Taubert et al30, 2003, Germany</td>
<td>Crossover, 14 d/phase (isolated systolic hypertension stage I), no medication</td>
<td>15 (67), 58.8 (55-64)</td>
<td>10, No funding</td>
<td>Dark chocolate (100 g/d containing 500 mg of polyphenols) vs polyphenol-free white chocolate; energy: 480 kcal/d</td>
<td>Cocoa: 153.3 (4.4)/148.6 (2.4); Control: 153.6 (4.4)/154.0 (3.6)</td>
<td>Cocoa: 84.5 (4.6)/82.9 (4.6); Control: 84.2 (4.2)/84.5 (4.3)</td>
</tr>
<tr>
<td>Engler et al31, 2004, United States</td>
<td>Parallel group, 2 wk (healthy, normotensive subjects), no medication</td>
<td>21 (11/10), 32.1 (21-55)</td>
<td>10, Institutional grant: University of California, San Francisco, School of Nursing, Coca Research Institute, Vienna, Va</td>
<td>High-flavonoid chocolate (46 g/d containing 213 mg of procyanidins) vs low-flavonoid chocolate; energy: 240 kcal/d</td>
<td>Cocoa: 121.0 (5.4)/120.0 (4.0); Control: 112.8 (2.8)/110.0 (2.0)</td>
<td>Cocoa: 68.1 (2.5)/69.0 (2.0); Control: 66.1 (1.7)/66.0 (2.0)</td>
</tr>
<tr>
<td>Grassi et al32, 2005, Italy</td>
<td>Crossover, 15 d/phase (healthy, normotensive subjects), no medication</td>
<td>15 (7/8), 33.9 (SD, 7.6)</td>
<td>9, No funding</td>
<td>Dark chocolate (100 g/d containing 500 mg of polyphenols) vs polyphenol-free white chocolate; energy: 480 kcal/d</td>
<td>Cocoa: 109.3 (8.4)/102.7 (6.4); Control: 109.2 (7.7)/109.3 (7.2)</td>
<td>Cocoa: 71.6 (5.1)/67.5 (4.2); Control: 71.6 (5.2)/71.0 (4.8)</td>
</tr>
<tr>
<td>Grassi et al33, 2005, Italy</td>
<td>Crossover, 15 d/phase (essential hypertension grade I), no medication</td>
<td>20 (10/10), 43.7 (SD, 7.8)</td>
<td>9, No funding</td>
<td>Dark chocolate (100 g/d containing 500 mg of polyphenols) vs polyphenol-free white chocolate; energy: 480 kcal/d</td>
<td>Cocoa: 135.5 (5.8)/123.6 (6.3); Control: 135.6 (5.5)/134.7 (4.7)</td>
<td>Cocoa: 88.0 (4.1)/79.6 (5.4); Control: 87.6 (4.3)/87.5 (4.6)</td>
</tr>
<tr>
<td>Fraga et al34, 2005, Argentina</td>
<td>Crossover, 14 d/phase (healthy, normotensive subjects), no medication</td>
<td>28 (28/0), 18 (18-20)</td>
<td>8, Institutional grant: University of Buenos Aires and Agencia Nacional de Promocion Tecnica y Empresarial en la Ciencia y la Tecnologia (ANPCYT), Buenos Aires, Argentina</td>
<td>Flavanol-containing milk chocolate (105 g/d with 294 mg of flavonols and procyanidins) vs cacao butter chocolate (containing &lt;1 mg of flavonols); energy intake: 544 kcal/d (value provided by Mars Inc., McLean, Va)</td>
<td>Cocoa: 123 (3)/117 (2); Control: 123 (3)/121 (2)</td>
<td>Cocoa: 72 (2)/67 (2); Control: 71 (2)/70 (2)</td>
</tr>
</tbody>
</table>

Abbreviations: DBP, diastolic blood pressure; SBP, systolic blood pressure.

*If age range was not reported, standard deviation is given. There were no dropouts except in the study by Engler et al31 (1 dropout per-protocol analysis).
of 343 individuals allocated to tea (n = 171) and control (n = 172) arms. The median duration of the interventions in the cocoa studies was 2 weeks, and in the tea studies, 4 weeks. Of the cocoa and tea study participants, 63.9% and 70.7%, respectively, were men and 34.0% and 48.8%, respectively, had hypertension or high-normal blood pressure.

Of 5 cocoa studies, 4 reported a reduction of SBP and DBP after cocoa consumption. Compared with the cocoa-free control, the pooled decrease was −4.7 mm Hg (95% CI, −7.6 to −1.8 mm Hg; P = .002) in SBP and −2.8 mm Hg (95% CI, −4.8 to −0.8 mm Hg; P = .006) in DBP for cocoa intake (Figure 2). Of the 5 studies on tea consumption, none was associated with significant alterations in blood pressure. Compared with control, the pooled change was 0.4 mm Hg (95% CI, −1.3 to 2.2 mm Hg; P = .63) in SBP and −0.6 mm Hg (95% CI, −1.5 to 0.4 mm Hg; P = .38) in DBP for tea intake (Figure 3).

There was evidence of considerable heterogeneity between the cocoa studies with respect to SBP (Q = 32.33; P = .001; I² = 87.6%) as well as DBP (Q = 32.18; P = .001; I² = 87.6%). In contrast, there was no indication of heterogeneity between the tea studies (SBP: Q = 0.61; P = .96; I² = 0%; and DBP: Q = 3.29; P = .51; I² = 0%). Exclusion sensitivity analysis showed that heterogeneity was due to the studies by Engel et al and Grassi et al. Omitting these studies had little impact on the pooled estimates for changes in SBP (~4.5 mm Hg [95% CI, −5.5 to −3.5 mm Hg]; P < .001) and DBP (−3.1 mm Hg [95% CI, −3.8 to −2.3 mm Hg]; P < .001).

Additional sensitivity analysis demonstrated that the values for the pooled changes in blood pressure with corresponding CIs and
Table 2), with a mean (SD) of 9.2 (2.8) and 9.4 (2.9), respectively.

Table 3 presents the pooled and individual changes in SBP and DBP due to cocoa intake in controlled randomized studies. The results suggest that younger normotensive subjects show larger reductions (Table 1). Moreover, it appears that the amount of the ingested cocoa phenols is essential for the magnitude of the blood pressure reduction, since in the study by Engler et al, administration of about half of the cocoa phenols over the same 2-week period did not affect blood pressure.

COMMENT

In our meta-analysis of randomized controlled trials in adults, diets rich in cocoa were associated with statistically significant reductions in SBP and DBP, whereas black or green tea did not lead to apparent changes in blood pressure. The magnitude of the hypotensive effects of cocoa is clinically noteworthy; it is in the range that is usually achieved with monotherapy of β-blockers or angiotensin-converting enzyme inhibitors. At the population level, a reduction of 4 to 5 mm Hg in SBP and 2 to 3 mm Hg in DBP would be ex-

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The blood pressure–lowering effects of cocoa have a biological basis. Cocoa is a rich source of polyphenols. In mechanistic studies, cocoa extracts have been shown to cause arterial vasodilation by increasing endothelial production of nitric oxide. In clinical studies in healthy subjects, infusion of the nitric oxide synthase inhibitor NG-nitro-L-arginine methyl ester (L-NAME) caused doubling of SBP and DBP responses after consumption of cocoa. These studies suggest that the dilator responses of the tea polyphenols are outweighed by pressor effects of the tea caffeine, since administration of caffeine-matched control beverages had no sustained impact (ie, lasting more than 60 minutes after consumption) on blood pressure. However, the composition of the polyphenols differs between cocoa and tea. The main polyphenol monomers in black and green tea are flavan-3-ols (in particular epicatechin gallates) and gallic acid, the main polymers are condensed catechins (in particular, thearubigins and theaflavins) that dominate in black tea. The flavan-3-ols epicatechin and catechin are also present in cocoa, but the main cocoa polyphenols are procyanidins. Whereas the flavanols or gallic acid were found to exhibit no or only modest vasodilatory or nitric oxide–stimulating effects in different experimental settings and there are no data on vascular effects of thearubigins and theaflavins, the fraction of oligomeric procyandin oligomers demonstrated a strong vasodilatory effect. Furthermore, in humans, bioavailability of phenolic compounds from cocoa has been reported not only for the monomeric flavanols but also for the procyanidin oligomers. This suggests that the different plant phenols must be differentiated with respect to their blood pressure–lowering potential and thus cardiovascular disease prevention, supposing that the tea phenols are less active than cocoa phenols. In support of this conclusion, results of a component-based epidemiological study have shown that dietary flavanol intake was not associated with the incidence of myocardial infarction and stroke, while other flavonoids were found to be protective.

We pooled the data of black and green tea interventions in a single meta-analysis because the principal polyphenol components are all
most identical in black and green tea, and, although the relation of these components may vary between black and green tea, total polyphenols are in a similar concentration range.47

The present study provides robust effect estimates. The prospective design of the meta-analysis minimizes selection and recall biases. Despite residual statistical heterogeneity between the cocoa studies, the adjustments made by sensitivity analyses revealed no significant changes in pooled outcome measures.

Our findings have several potential limitations. First, as with any meta-analysis the internal validity relies on the quality of the individual studies. Although all studies were randomized and described adverse events or withdrawals, the lack of blinding of participants or investigators to the intervention in most of the studies reviewed increased the risk of expectation bias.

Second, our meta-analysis involved only a few studies with small sample sizes, which makes the estimates especially susceptible to publication bias and to overestimation of treatment effects; consequently, accuracy and statistical power of the outcome estimates were limited.59 Although the Egger regression test and trim-and-fill computation provided no indication of publication bias, this cannot be ruled out because these tests lacked sensitivity, with the inclusion of only 5 studies in our meta-analysis.

Third, the studies reviewed had only a short duration. Thus, their results cannot simply be translated into long-term outcomes, that is, the prediction of beneficial treatment effects. In particular, it has to be considered that the short-term administration and the calorie-balanced study design prevented a potential weight gain with the high-caloric cocoa diets (Table 1); however, a concurrent increase in body weight may reverse any blood pressure reductions during long-term habitual intake of cocoa products.60 Although outcome evidence from long-term randomized trials is ideal, those studies with dietary interventions are difficult to implement on a practical basis. It is therefore instructive to compare the data of our meta-analysis with the results of long-term observational studies.

A recent cross-sectional study that assessed habitual cocoa intake and blood pressure in 470 elderly men over 5 years found a −3.7 mm Hg (95% CI, −7.1 to −0.3 mm Hg) lower mean SBP and a −2.1 mm Hg (95% CI, −4.0 to −0.2 mm Hg) lower mean DBP in the highest tertile of cocoa intake compared with the lowest tertile.12 This is close to the pooled estimates we derived from the randomized trials but was observed with one tenth of the daily cocoa amount compared with the intake in the randomized trials. Hence, the long-term effects of high cocoa consumption on blood pressure may be underestimated by the presented meta-analysis of short-term trials. Moreover, the high degree of risk re-
duction of about 50% in cardiovascular and all-cause mortality associated with regular cocoa intake suggests that cocoa phenols also confer genuine cardiovascular protection beyond blood pressure reduction, possibly due to protective nitric oxide–mediated effects on endothelium or platelets.

In contrast, long-term epidemiological studies of tea intake and blood pressure reported either no blood pressure–lowering effects of habitual tea consumption or only small reductions of approximately −2 mm Hg in SBP and −1 mm Hg in DBP, which is consistent with the nonsignificant effects in the short-term randomized trials. Accordingly, a meta-analysis of observational studies on tea consumption in relation to cardiovascular disease conducted in 2001 found only a small, nonsignificant reduction of myocardial infarction incidence with an increase in tea consumption of 3 cups per day (relative risk, 0.89; 95% CI, 0.79 to 1.01). Subsequent population studies also reported no or similar modest inverse associations of regular tea intake and cardiovascular diseases.

In conclusion, controlled data from short-term randomized and long-term observational studies suggest clinically relevant reductions of SBP and DBP with the use of cocoa products, supported by the biological plausibility and consistent laboratory data of the vasodilator activity of cocoa phenols. In contrast, cumulative evidence does not support substantial effects of tea consumption on blood pressure. The findings of favorable hypotensive cocoa actions should, however, not encourage common recommendations to consume more cocoa. We believe that any dietary advice must account for the high sugar, fat, and calorie intake with most cocoa products. On the basis of the limitations of current dietary studies, it appears reasonable to allow phenol-rich cocoa products such as dark chocolate for calorie-balanced substitution of high-fat dairy products, sugar confectionary, or cookies of the usual diet. Rationally applied, cocoa products might be considered part of dietary approaches to lower hypertension risk.

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Author Contributions: Dr Taubert had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis. Study concept and design: Taubert. Acquisition of data: Taubert and Roesen. Analysis and interpretation of data: Taubert, Roesen, and Schomig. Drafting of the manuscript: Taubert. Critical revision of the manuscript for important intellectual content: Taubert, Roesen, and Schomig. Statistical analysis: Taubert. Administrative, technical, and material support: Schomig. Study supervision: Taubert.

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REFERENCES


